UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/582,337	09/18/2000	Takuya Tamatani	SHIM-006	8342

24353 7590 09/10/2002

BOZICEVIC, FIELD & FRANCIS LLP
200 MIDDLEFIELD RD
SUITE 200
MENLO PARK, CA 94025

EXAMINER
HUYNH, PHUONG N

ART UNIT	PAPER NUMBER
1644	16

DATE MAILED: 09/10/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/582,337	Applicant(s) TAMATANI ET AL.	
	Examiner " Neon" Phuong Huynh	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 June 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *104-108, 121, 123, 127-135 and 142* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *104-108, 121, 123, 127-135, and 142* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Claims 104-108, 121, 123, 127-135, and 142 are pending.

2. In view of the amendment filed 6/10/02, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 104-108, 121, 123, 127-135 and 142 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the hybridomas FERM BP-6208 and BP-6209 in claims 105-108 and 127 and kidney-derived fibroblast cell line 293-T (ATCC CRL 1573) recited in claim 155 are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, a deposit of the hybridomas, which produce these antibodies, may satisfy first paragraph. See 37 CFR 1.801-1.809.

It is noted that hybridomas FERM BP-6208 and BP-6209 have been deposited as indicated on page 75 of the specification. However, it is not apparent if the deposit has been made under the terms of the Budapest Treaty.

If the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the hybridomas FERM BP-6208 and BP-6209 have been deposited under the Budapest Treaty and that the hybridomas will be irrevocably and without restriction or condition released to the public upon the issuance of a patent would satisfy the deposit requirement made herein. See 37 CFR 1.808. Further, the record must be clear that the deposit will be maintained in a public

depository for a period of 30 years after the date of deposit or 5 years after the last request for a sample or **for the enforceable life of the patent whichever is longer**. See 37 CFR 1.806.

If the deposit has not been made under the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature must be made, stating that the deposit has been made at an acceptable depository and that the criteria set forth in 37 CFR 1.801-1.809, have been met.

It is noted that kidney-derived fibroblast cell line 293-T (ATCC CRL 1573) is commercially available from ATCC as indicated on page 83 of the specification. The Office will accept commercial availability as evidence that a biological material is known and readily available only when the evidence is clear and convincing that the public has access to the material. See the final rule entitled "Deposit of Biological Materials for Patent Purposes," 54 FR 34864, 34875 (August 22, 1989). A product could be commercially available but only at a price that effectively eliminates accessibility to those desiring to obtain a sample.

The specification does not reasonably provide enablement for (1) *any* non-human monoclonal antibody or portion thereof which is reactive to human, mouse and rat connective tissue growth factors (CTGFs) as recited in claim 104, (2) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6208 as recited in claim 106, (3) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6209 as recited in claim 108, (4) *any* cell producing *any* non-human monoclonal antibody as recited in claim 121, (4) *any* hybridoma obtainable by fusing a mammalian myeloma cell with a mammalian B cell which is capable of producing any non-human monoclonal antibody as recited in claim 123, (5) *any* antibody-immobilized insoluble carrier as recited in claim 128, (6) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is selected from the group consisting of plates, test tubes, tubes, beads, balls, filters, and membrane as recited in claim 129, (7) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is a filter or membrane, or that used for affinity column chromatography as recited in claim 130, (8) *any* labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with any other substances as

recited in claim 131, (9) *any* labeled non-human antibody wherein said labeling agent is an enzyme, fluorescent substance, chemiluminescent substance, biotin, avidin, or radioisotope as recited in claim 132, (10) a kit for detecting or assaying any mammalian CTGF comprising *any* non-human monoclonal antibody or portion thereof as recited in claim 133, (11) a kit for detecting or assaying any mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which the said non-human monoclonal antibody is immobilized as recited in claim 134, (12) a kit for detecting or assaying *any* mammalian CTGF comprising a labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with *any* other substances as recited in claim 135, (13) a kit for separating or purifying *any* mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which *any* non-human monoclonal antibody is immobilized as recited in claim 142 and (14) *any* non-human monoclonal antibody or a portion thereof characterized by inhibiting the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573) for detection assays as recited in claim 155.

The specification discloses only (1) a mouse anti-human CTGF monoclonal antibody produced by hybridoma BP-6208 (clone 8-86-2) that cross-reacts with human, mouse and rat connective tissue growth factor (CTGF) (See page 99, lines 15-16, Fig 1) and (2) a mouse anti-human CTGF monoclonal antibody that produced by hybridoma BP-6209 (clone 8-64-6) that cross-reacts with human and mouse CTGF (See page 98, lines 30-34, Fig 1). Both antibodies inhibit the binding of human CTGF to human 293 fibroblast (Fig 1 and Fig 5-7) for detection assays such as ELISA (See page 99-102, Fig 21). The specification discloses additional antibodies such as the ones listed in Figs 1 & 2. However, not every antibody listed in Fig 1&2 has the same properties as the claimed antibodies produced by hybridoma BP-6208 and hybridoma BP-6209. The specification discloses only a full-length rat CTGF polypeptide consisting of SEQ ID NO: 2 and human CTGF polypeptides consisting of SEQ ID NOS: 5-16, 18, 20, 22 and 24. The specification does not provide any guidance as how to make and use *any* antibody that binds to *any* mammalian CTGF other than the specific CTGF mentioned above. There is insufficient information regarding to the epitope (specific amino acid residues) to which the antibody binds and whether the binding specificity is sequential or conformational dependent.

Kuby *et al,* of record, teach that antibody epitopes (B cell epitopes) are not linear and are comprised of complex three-dimensional array of scattered residues which will fold into specific conformation that contribute to binding (See Kuby 1994, page 94, in particular). Immunization

with a peptide fragment derived from a full-length polypeptide may result in **antibody specificity** that differs from the antibody specificity directed against the native full-length polypeptide. Given the indefinite number of undisclosed antibody encompassed by the claims, it is unpredictable which undisclosed antibody would bind to just any mammalian CTGFs and would have the same functional characteristics as monoclonal antibody produced by hybridoma BP-6208 and hybridoma BP-6209 such as inhibiting the binding of human CTGF to 293 fibroblast. It follows that *any* cell or hybridoma producing *any* undisclosed non-human monoclonal antibody is not enable. It also follows that *any* labeled undisclosed non-human monoclonal antibody or portion thereof and kit comprising *any* undisclosed non-human monoclonal antibody are not enabled.

For these reasons, the specification as filed fails to enable one skill in the art to practice the invention without undue amount of experimentation. As such, further research would be required to practice the claimed invention.

Applicants' arguments filed 6/10/02 have been fully considered but are not found persuasive.

Applicants' position is that (1) A "statement of Availability" is attached hereto, (2) Also, applicants have attached a copy of a catalog that shows details of the cell line available from ATCC, (3) Claim 104 has been amended to show that it does not intended to cover all the non-human antibodies that bind to any of mammalian CTGFs, As Fig 1 of the present applications shows, many embodiments within this genus other than 8-64-6 (FERM BP-6209), 8-86-2 (FERM BP-6208), namely 8-97-3, 8-149-3, 15-38-1, 17-132, 24-53, 24-67 and 2-228-1, have been demonstrated. Thus, Applicants have discloses a representative number of species in the claimed genus as required by law.

However, the "Statement of Availability" and a copy of a catalog that shows details of the cell line available from ATCC are not found. The amended claims still read on any non-human monoclonal antibody or portion thereof which (a) that binds to (cross-react with) all of human, mouse and rat connective tissues growth factors (CTGFs) and (b) has the IgG isotype. Further, there is insufficient guidance and working example demonstrating any undisclosed non-human monoclonal or a portion thereof can inhibit the binding of human CTGF to human kidney-derived fibroblast such as 293-T (ATCC CRL 1573). Finally, there is insufficient guidance as to which "portion thereof" of any undisclosed non-human monoclonal or a portion thereof can

inhibit the binding of human CTGF to human kidney-derived fibroblast such as 293-T (ATCC CRL 1573).

5. Claims 104, 106, 108, 121, 123, 128-135 and 142 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification discloses only (1) a mouse anti-human CTGF monoclonal antibody produced by hybridoma BP-6208 (clone 8-86-2) that cross-reacts with human, mouse and rat connective tissue growth factor (CTGF) (See page 99, lines 15-16, Fig 1) and (2) a mouse anti-human CTGF monoclonal antibody that produced by hybridoma BP-6209 (clone 8-64-6) that cross-reacts with human and mouse CTGF (See page 98, lines 30-34, Fig 1). Both antibodies inhibit the binding of human CTGF to human 293 fibroblast (Fig 1 and Fig 5-7) for detection assays such as ELISA (See page 99-102, Fig 21).

The specification does not reasonably provide a **written description** of (1) *any* non-human monoclonal antibody or portion thereof which is reactive to human, mouse and rat connective tissue growth factors (CTGFs), (2) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6208, (3) *any* non-human monoclonal antibody or portion thereof comprises *any* property substantially equivalent to that of a monoclonal antibody produced by a hybridoma identified by international deposit accession No. FERM BP-6209, (4) *any* cell producing *any* non-human monoclonal antibody, (4) *any* hybridoma obtainable by fusing a mammalian myeloma cell with a mammalian B cell which is capable of producing any non-human monoclonal antibody, (5) *any* antibody-immobilized insoluble carrier, (6) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is selected from the group consisting of plates, test tubes, tubes, beads, balls, filters, and membrane, (7) *any* non-human antibody-immobilized insoluble carrier wherein said carrier is a filter or membrane, or that used for affinity column chromatography, (8) *any* labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with any other substances, (9) *any* labeled non-human antibody wherein said labeling agent is an enzyme, fluorescent substance, chemiluminescent substance, biotin, avidin, or radioisotope, (10) a kit for

detecting or assaying any mammalian CTGF comprising *any* non-human monoclonal antibody or portion thereof, (11) a kit for detecting or assaying any mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which the said non-human monoclonal antibody is immobilized, (12) a kit for detecting or assaying *any* mammalian CTGF comprising a labeled antibody which is prepared by labeling *any* non-human monoclonal antibody or a portion thereof with a labeling agent capable of providing a detectable signal by itself or together with *any* other substances (13) a kit for separating or purifying *any* mammalian CTGF comprising *any* antibody-immobilized insoluble carrier on which *any* non-human monoclonal antibody is immobilized and (14) *any* non-human monoclonal antibody or a portion thereof characterized by inhibiting the binding of human CTGF to human kidney-derived fibroblast cell line 293-T (ATCC CRL1573) for detection assays.

With the exception of monoclonal antibodies that produced by the hybridomas mentioned above, there is no description about the structure associated with function of *any* connective tissue growth factors (CTGFs) to which the antibody binds. Further, the specification fails to describe additional representative species of non-human monoclonal antibody that binds to just about *any* CTGFs. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Given the lack of description and the lack of additional representative species as encompassed by the claim, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.* Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' position is that (1) Claim 104 has been amended to show that it does not intended to cover all the non-human antibodies that bind to any of mammalian CTGFs. The antibody claimed has to bind to all three CTGFs, namely human, rat and mouse CTGFs; (2) As Fig 1 of the present applications shows, many embodiments within this genus other than 8-64-6 (FERM BP-6209), 8-86-2 (FERM BP-6208), namely 8-97-3, 8-149-3, 15-38-1, 17-132, 24-53, 24-67 and 2-228-1, have been demonstrated. Thus, Applicants have discloses a representative number of species in the claimed genus as required by law.

However, the amended claims still read on any non-human monoclonal antibody or portion thereof which (a) that binds to (cross-react with) all of human, mouse and rat connective tissues growth factors (CTGFs) and (b) has the IgG isotype where connective tissue growth factor

is any CTGFs such as TGFbeta, PDGF, FGF, and EGF. The amended claims still read on any non-human monoclonal antibody or portion thereof which (a) that binds to (cross-react with) all of human, mouse and rat connective tissues growth factors (CTGFs) and (b) has the IgG isotype. Further, there is insufficient written description about any undisclosed non-human monoclonal or a portion thereof can inhibit the binding of human CTGF to human kidney-derived fibroblast such as 293-T (ATCC CRL 1573). Finally, it is not clear which "portion thereof" of the undisclosed non-human monoclonal can inhibit the binding of human CTGF to human kidney-derived fibroblast such as 293-T (ATCC CRL 1573).

6. Claims 108 and 127 are free of prior art.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

10. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

Phuong N. Huynh, Ph.D.
Patent Examiner
Technology Center 1600
Sept 9, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600